

Remarks

Claims 1-56 were pending in the application. Claims 5, 6, 23, 29, 31, 32, 36, 37, 39-56 are canceled. Claims 1-4, 7-22, 24-26, 30, 33-35, and 38 stand rejected, and claims 27 and 28 have been objected to as depending from a rejected claim. Claims 1-3, 12-19, 21, 22, 24-26, 33, 38 are amended as above. New claims 57-62 have been added. Support for new claim 57 can be found on page 13, line 6, through page 13, line 17, and in Figure 15; support for new claim 58 can be found on page 10, lines 9-15; and support for claims 59-62 can be found, for example, on page 57, line 15 – page 58, line 25. Applicant submits that no new matter has been added by these amendments. Applicant respectfully requests reexamination and reconsideration of the case, as amended. Each of the rejections levied in the Office Action is addressed individually below.

I. **Rejection under 35 U.S.C. §112, first paragraph, for lack of enablement.** Claims 30, 33-35, and 38 stand rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. The Examiner has stated that the scope of the method claims are not adequately enabled solely based on the inhibitory effect of the inventive compounds on the Hsp90 molecular chaperone. In light of the inhibitory effect of the inventive compounds on the Hsp90 molecular chaperone, the independent claims 30, 33, and 38 have been amended to recite treating Hsp90-dependent cancers, or inhibiting or killing Hsp90-dependent cancer cells. As the Examiner has indicated, the inventive compounds have been shown by the inventors to inhibit the Hsp90 molecular chaperone. Therefore, the specification does enable one of ordinary skill in this art to treat Hsp90-dependent cancers or kill or inhibit Hsp90-dependent cancer cells. Applicant submits that the amended claims are fully enabled and requests that the rejection be removed.

New claims 59-61 have also been added that create methods of killing cancer cells that do not express retinoblastoma. In light of the evidence presented in the Specification, Applicant respectfully submits that these claims are also fully enabled.

II. Rejection under 35 U.S.C. § 112, second paragraph, as being indefinite. Claims 1-4, 7-22, 24-28, 30, 33-35, and 38 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- a) All occurrences of the phrase “protecting group” have been removed from the pending claims as requested by the Examiner. Applicant submits that the amended claims are definite.
- b) Claim 1 has been amended to remove the moiety $-C(O)NR_K$ from the definition of R_7 . Applicant submits that claim 1 is now definite.
- c) All occurrences of the phrases “analogues of radicicol and monocillin” and “analogues of geldanamycin” have been removed from the pending claims. Applicant submits that the claims are definite and requests that the rejection be removed.
- d) Claim 1 has been amended to make the definition of R_L definite by reciting “alkenyl” and “acyl” moieties rather than alkylene moiety and carbonyl moiety, respectively. Both alkenyl and acyl moieties are monovalent, therefore, fitting with R_L being a monovalent substituent. Applicant requests that the rejection be removed.
- e) Periods have been added to the ends of claims 1, 22, and 24-26 as requested by the Examiner. Applicant apologizes for this inadvertent error in the claims.
- f) Applicant has amended the $-OS(=O)OR_J$ moiety in the definition of R_5 and R_6 to be $-OSO_2R_J$ in order to be more clear and provide antecedent basis for the same moiety recited in claim 19.
- g) The structure in claim 24 has been amended to recite explicitly the exocyclic methylene group. Applicant submits that the claim is definite and requests that the rejection be removed.

III. Rejections under 35 U.S.C. § 102.

Claims 1, 4, 7, 13, 18, and 21 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Mirrington *et al.* (*Tetrahedron Letters* 7:365-370 (1964)). Examiner states that Mirrington *et al.* teaches the compounds of the instant invention where Z is O; X is O; A and B

taken together are oxirano; R₅ and R₆ are H; D and E taken together are –CH₂-CH₂-; G and J taken together are –CH₂-CH₂-; K and L taken together are C=O; R₁ is Cl; R₂ is OH or OMe; R₃ is H; and R₄ is OH and OMe. Applicant has amended claim 1 to exclude compound II on page 366 of the paper by Mirrington *et al.* (see proviso at end of claim 1). Applicant, therefore, submits that Mirrington *et al.* do not anticipate the claimed invention and requests that the rejection be withdrawn.

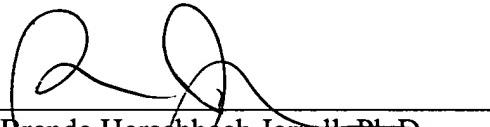
Claims 1, 4, 13, 18, 21, 30, 33-35, and 38 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Sugimura *et al.* (U.S. Patents 5,650,430 and 5,597,846). Examiner states that Sugimura teaches compounds wherein Z is O; X is O; A and B together are oxirane; R₅ and R₆ are H; D and E together are –CH=CH-; G and J together are –CH=CH-; K and L together are C=O; R₁ is Cl; R₂ is OR_B or O(C=O)R_B; R₃ is H, and R₄ is OR_D or O(C=O)R_D where R_B and R_D are arylalkyl, heteroaryl, etc. Originally filed claim 1, however, excluded such compounds from the claimed invention (see proviso on lines 10-17 of page 89). Applicant, therefore, submits that the claimed invention is not anticipated by the claimed invention.

Lastly, claims 1, 4, 7, 13, 18, 21, and 30 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Lampilas *et al.* (*Tetrahedron Letters*, 33(6):773-776, 777-780, 1992). The Examiner states that Lampilas *et al.* teach the compounds wherein Z is O; X is O; A and B taken together are oxirane; R₅ and R₆ are H; D and E taken together are –CH=CH-; G and J taken together are –CH=CH-; K and L taken together are C=O; R₁ is H or Cl; R₂ is OH or *tert*-butyldimethylsilyloxy; R₃ is H; and R₄ is *tert*-butyldimethylsilyloxy. Again, these compounds which include monocillin I and radicicol were provisoed out of the originally filed claim 1 (see lines 10-17 of page 89). Therefore, Lampilas *et al.* do not anticipate the claimed invention, and Applicant requests that the rejection be removed.

In view of the forgoing amendments and arguments, Applicant respectfully submits that the present case is now in condition for allowance. A Notice to that effect is requested.

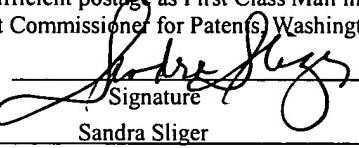
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Respectfully submitted,



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